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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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EXAMINER
HADDAD, MAHER M

ART UNIT	PAPER NUMBER
1644	

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Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/732,754	DRUILHE ET AL.	
	Examiner	Art Unit	
	Maher M. Haddad	1644	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☐ Responsive to communication(s) filed on *3-05-02* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-25* is/are pending in the application.

4a) Of the above claim(s) *1-9, 15 and 20-24* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *10-14, 16-19 and 25* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a)☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1)☒ Notice of References Cited (PTO-892)
2)☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3)☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4)☐ Interview Summary (PTO-413) Paper No(s). _____ .
5)☐ Notice of Informal Patent Application (PTO-152)
6)☐ Other: .

DETAILED ACTION

1. Upon further consideration Groups II-III have been rejoined with Group I. Groups V-VI have been rejoined with Group IV.

2. Applicant's election with traverse of Group IV (claims 10-14, 16-19 and 25) filed on 3-5-2002 is acknowledged.

The traversal is on the ground(s) that the Office has characterized the relationship between Groups IV-VI and I-III as product and process of use. The office concluded that the product as claimed can be used as an immunogen to make an antibody but the office did not provide reasons and /or examples to support this conclusion. This is not found persuasive because Groups I-III and IV-VI are classified in different Classes and are recognized divergent subject matter. Specifically, Groups I-III recite methods of inducing an immune response using a lipid-tailed polypeptide of Group IV-VI respectively. In addition, they are classified differently which would require different search.

The requirement is still deemed proper and is therefore made FINAL.

Claims 1-9, 15, and 20-24 are withdrawn from further consideration by the Examiner, 37 C.F.R. § 1.142(b) as being drawn to a nonelected invention.

Claims 10-14, 16-19 and 25 *are under consideration in the instant application.*

3. Applicant's IDS, filed 12-11-2000 and 10-09-01, are acknowledged.

The AO reference cited on the form PTO-1449 filed on 12/11/00 was considered only in regard to the English Abstract, as the entire document was not translated. In addition, the AO reference cited on PTO-1449 filed on 10-09-01 was crossed out because the entire document was not translated. Applicant is invited to produce such translation.

4. A. The disclosure is objected to because the word "fro" in page 4, lines 21 and 30, the word "electited" in page 4, line 25, the word "IFI" in page 4, line 23, and the word "regiospecific" in page 12, line 2 are misspelled.

B. The disclosure is objected to because the "Material and Methods" referred to in page 4, line 23 was not found in the disclosure.

5. The following is a quotation of the second paragraph of 35 U.S.C. 112.

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

6. Claims 10-11, 13, 16, 18-19 and 25 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

A) It is indefinite and ambiguous to recite "in [the] absence of toxic adjuvant" in claims 10 and 16. Said phrase implies 'in the present of non-toxic adjuvant". The specification discloses the use of the composition without the adjuvant.

B) Claims 10, and 16-17 are generally narrative and indefinite, failing to conform with current U.S. practice. They appear to be a literal translation into English from a foreign document and are replete with grammatical and idiomatic errors. It is improper to recite "consisting in at least one". Also, the recitation of "in absence of" is improper, Applicant is invited to rephrase the citation to "in the absence of".

C) The "the lipopeptide" recited in claim 13 has no antecedent basis in base claims 11 and 10. Base claims 10 and 11 recite a composition.

D) It is indefinite and ambiguous to recite a "composition comprising lipid-tailed polypeptide or peptide" in claim 25, line 1. It is suggested that said phrase be changed to "composition comprising a lipid-tailed polypeptide or peptide".

E) The "absence of toxic adjuvant" and "the absence of adjuvant" recited in claims 16 and 18 respectively have no antecedent basis in base claims 13 and 11. Base claim 11 recite the adjuvant is non-toxic.

7. The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

8. Claims 10-13, 16-19 and 25 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a composition consisting of at least one lipoprotein of SEQ ID NOS: 1-3 for *in vivo* induction of both B- and T-cell responses, does not reasonably provide enablement for any other composition consisting of at least one lipoprotein for any other mucosal immune response; any lipopeptide, wherein the lipopeptide is tailed with any lipid component; any vaccine composition for mucosal administration containing at least one lipopeptide inducing any B and/or T cell response in vivo in absence of adjuvant; any vaccine composition containing any lipopeptide; any immunogenic composition containing any lipopeptide; or any composition comprising lipid-tailed polypeptide or peptide, said lipid-tailed peptide having at least any lipid residue bound to any epitope T amino acid sequence and optionally at least one epitope B amino acid sequence. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

Factors to be considered in determining whether undue experimentation is required to practice the claimed invention are summarized *In re Wands* (858 F2d 731, 737, 8 USPQ2d 1400, 1404 (Fed. Cir. 1988)). The factors most relevant to this rejection are the scope of the claim, the amount of direction or guidance provided, the lack of sufficient working examples, the unpredictability in the art and the amount of experimentation required to enable one of skill in the art to practice the claimed invention.

The specification disclosure is insufficient to enable one skilled in the art to practice the invention as broadly claimed without an undue amount of experimentation.

Other than the specific SEQ ID NOS: 1-3 mentioned above for induction of both B- and T-cell responses, the specification fails to provide any guidance as how to make and use any composition consisting of at least one lipoprotein for any mucosal immune response; any lipopeptide, wherein the lipopeptide is tailed with any lipid component; any vaccine composition for mucosal administration containing at least one lipopeptide inducing any B and/or T cell response in vivo in absence of adjuvant; any vaccine composition containing any lipopeptide; any immunogenic composition containing any lipopeptide; or any composition comprising lipid-tailed polypeptide or peptide, said lipid-tailed peptide having at least any lipid residue bound to any epitope T amino acid sequence and optionally at least one epitope B amino acid sequence. There is insufficient guidance as to which amino acid residue within the lipoprotein, or the lipopeptide mentioned above can be deleted, substitute and whether the resulting lipoprotein or lipopeptide would maintain the function as SEQ ID NOS:1-3. Ngo *et al* teach that the amino acid positions within the polypeptide/protein that can tolerate change such as conservative substitution or no substitution, addition or deletion which are critical to maintain the protein's structure/function will require guidance (see Ngo et al., 1994, The Protein Folding Problem and Tertiary Structure Prediction, pp. 492-495). Given the lack of sufficient guidance and working examples, predicting what changes can be made to the amino acid sequence of SEQ ID NOS: 1-3 that after substitution, deletion, insertion

and/or modification will retain both structure and have similar function as SEQ ID NOS: 1-3 is unpredictable. *In re Fisher*, 166 USPQ 18 indicates that the more unpredictable an area is, the more specific enablement is necessary in order to satisfy the statute. Since the amino acid sequence of a lipopeptide determined its structural and functional properties, predictability of which fragments will retain functionality requires knowledge of, and guidance with regard to, which amino acids in the lipopeptide's sequence contribute to its structure, and therefore, function.

The goal of vaccination is the induction of circulating specific antibodies to prevent the initial infection of the liver with the parasite. There is no sufficient guidance provided to assist one skilled in the art in the selection of all such possible vaccine containing any lipopeptide nor is there evidence provided that any lipoprotein or lipopeptide would be therapeutically effective. It appears that undue experimentation would be required of one skilled in the art to practice the claimed composition in providing effective vaccines to induce the circulating parasite specific antibodies.

Reasonable correlation must exist between the scope of the claims and scope of enablement set forth. In view of the quantity of experimentation necessary, the limited working examples, the unpredictability of the art, the lack of sufficient guidance in the specification, and the breadth of the claims, it would take undue trials and errors to practice the claimed invention.

9. Claims 10-13, 16-19 and 25 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Applicant is in possession of SEQ ID NOS: 1- 3 for the induction of B- and T-cell responses.

Applicant is not in possession of any other composition consisting of at least one lipoprotein for any other mucosal immune response; any lipopeptide, wherein the lipopeptide is tailed with any lipid component; any vaccine composition for mucosal administration containing at least one lipopeptide inducing any B and/or T cell response in vivo in absence of adjuvant; any vaccine composition containing any lipopeptide; any immunogenic composition containing any lipopeptide; or any composition comprising lipid-tailed polypeptide or peptide, said lipid-tailed peptide having at least any lipid residue bound to any epitope T amino acid sequence and optionally at least one epitope B amino acid sequence.

Applicant has disclosed only SEQ ID NOS: 1-3; therefore, the skilled artisan cannot envision all the contemplated amino acid sequence possibilities recited in the instant claims. Consequently, conception in the above cases cannot be achieved until a representative description of the structural and functional properties of the claimed invention has occurred, regardless of the complexity or simplicity of the method. Adequate written description requires more than a mere statement that it is part of the invention. The sequences themselves are required. See *Fiers v. Revel*, 25 USPQ2d 1601, 1606 (CAFC1993). The Guidelines for the Examination of Patent Application Under the 35 U.S.C.112, ¶ 1"Written Description" Requirement make clear that the written description requirement for a claimed genus may be satisfied through sufficient description of a representative number of species disclosure of relevant, identifying characteristics, i.e., structure or other physical and or chemical properties, by functional characteristics coupled with a known or disclosed correlation between function and structure, or by a combination of such identifying characteristics, sufficient to show the applicant was in possession of the genus (Federal Register, Vol. 66, No. 4, pages 1099-1111, Friday January 5, 20001, see especially page 1106 3rd column).

Given the lack of a written description of *any* additional representative species other than SEQ ID NOS: 1-3, one of skill in the art would reasonably conclude that the disclosure fails to provide a representative member of species to describe the genus. Thus applicant was not in possession of the claimed genus.

Vas-Cath Inc. v. Mahurkar, 19 USPQ2d 1111, makes clear that "applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession of the invention. The invention is, for purposes of the written description inquiry, whatever is now claimed." (See page 1117.) The specification does not "clearly allow persons of ordinary skill in the art to recognize that [he or she] invented what is claimed." (See Vas-Cath at page 1116.). Consequently, Applicant was not in possession of the instant claimed invention. See University of California v. Eli Lilly and Co. 43 USPQ2d 1398.

Applicant is directed to the Revised Interim Guidelines for the Examination of Patent Applications Under the 35 U.S.C. 112, ¶ 1 "Written Description" Requirement, Federal Register, Vol. 66, No. 4, pages 1099-1111, Friday January 5, 2001.

10. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless --

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

11. Claims 10, 12, 14, 16-18 and 25 are rejected under 35 U.S.C. 102(b) as being anticipated by Perlaza et al (July 1998).

Perlaza et al. teach a LSA1-J (the instant claimed SEQ ID NO: 2) and LSA-3 NRII (the instant claimed SEQ ID NO: 3) lipopeptides (the entire document and page 3424, table I in particular), as recited in claim 14, wherein the lipopeptide is tailed with a lipid component (page 3423, paragraph 1 right column in particular), as recited in claim 12.

Perlaza et al., further teach a vaccine composition of lipid-tailed peptides injected in phosphate-buffered saline without an adjuvant were used to immunized monkeys (in vivo) to develop an immune response (page 3423, paragraph 1 right column in particular), as recited in claims 10, 16-18 and 25. The immune response was demonstrated by the induction of both B and T cell response to the peptides (page 3423, see the Abstract in particular), as recited in the instant claim 17.

Furthermore, the reference teaches the peptides were derived from the *P. falciparum* pre-erthrocytic molecules contained T-cell epitopes (page 3424, right column paragraph 2 in particular) and the peptides were lipid-tailed peptides bound to a palmitic acid at the carboxyl-terminal end using a lysine residue as a linker (page 3423, right column paragraph 1 in particular), as recited in the instant claim 25.

The reference teachings anticipate the claimed invention.

12. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> *(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.*

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(f) or (g) prior art under 35 U.S.C. 103(a).

13. Claims 10-11, 13 and 19 are rejected under 35 U.S.C. 103(a) as being unpatentable over Perlaza et al. in view of U.S. Patent No. 6,251,405.

The Perlaza et al. reference, has been discussed, supra. The reference further teaches that the lipid component of the lipopeptide is a palmitoyl residue (page 3423, right column, paragraph 1 in particular) and the lipopeptides were able to produce immune response with high immunogenicity (page 3426, left column, paragraph 2 in particular), as recited in the instant claims 13 and 19 respectively.

The claimed invention differs from the reference teaching only by the recitation of a non-toxic adjuvant recited in claim 11.

The '405 patent teaches an immunological composition containing an adjuvant, wherein the lipoprotein is antigenic (entire docutment and column 3 lines 34-51 in particular). The '405 patent further teaches the characteristics of the ideal adjuvant, which include lack of toxicity (colume 2, lines 56-58 in particular) and immunogenicity can be significantly improved if an antigen is co-administered with an adjuvant (column 2, lines 22-23 in particular).

It would have been obvious to one of ordinary skill in the art at the time the invention was made to combine the non-toxic adjuvant taught by the '405 patent with the lipoprotein composition taught by Perlaza et al.

One of ordinary skill in the art at the time the invention was made would have been motivated to combine lipoprotein composition taught by Perlaza et al. with the non-toxic adjuvant taught by the '405 patent because immunogenicity of the composition can be significantly improved when a lipopolypeptide antigen is co-administered with a non-toxic adjuvant as taught by the '405 patent. Form the combined teachings of the references, it is apparent that one of ordinary skill in the art would have had a reasonable expection of success in producing the claimed invention.

Therefore, the invention as a whole was *prima facie* obvious to one of ordinary skill in the art at the time the invention was made, as evidenced by the references, especially in the absence of evidence to the contrary.

14. No claim is allowed.

15. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Maher Haddad, whose telephone number is (703) 306-3472. The examiner can normally be reached Monday to Friday from 8:00 to 4:30. A message may be left on the examiner's voice mail service. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Christina Chan can be reached at (703) 308-3973. Any inquiry of a general nature or relating to the status of this application should be directed to the Technology Center 1600 receptionist whose telephone number is (703) 308-0196.

Papers related to this application may be submitted to Technology Center 1600 by facsimile transmission. Papers should be faxed to Technology Center 1600 via the PTO Fax Center located in Crystal Mall 1. The faxing of papers must conform with the notice published in the Official Gazette, 1096 OG 30 (November 15, 1989). The CM1 Fax Center telephone number is (703) 305-3014.

Maher Haddad, Ph.D.
Patent Examiner
Technology Center 1600
March 21, 2002

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